UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,521	03/17/2004	Daniel P. Wermeling	INT-002C1CP	5461

51414 7590 01/27/2009

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
53 STATE STREET
EXCHANGE PLACE
BOSTON, MA 02109-2881

EXAMINER	
YU, GINA C	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
01/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PatentBos@goodwinprocter.com
hmcpeake@goodwinprocter.com
glenn.williams@goodwinprocter.com

Office Action Summary	Application No.	Applicant(s)	
	10/803,521	WERMELING, DANIEL P.	
	Examiner	Art Unit	
	GINA C. YU	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-15,17,18,20 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15, 17, 18, 20, 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/07/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of amendment filed on November 7th 2008. Claim rejections made under 35 U.S.C. 112, second paragraph and 103(a) as indicated in the previous Office action dated May 9, 2008 are withdrawn in view of applicant's amendment. Obviousness double patenting rejection is withdrawn in view of the claim amendment; new rejections are made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-15, 18, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 8-11, 19, 21, 23, 24, and 27 of US 6610271 in view of Schweizer (US 5,166,202).

The '271 patent claims a sedative-anxiolytic nasal composition comprising lorazepam; 15-25 % by volume of polyethylene glycol and 75-85 % by volume of propylene glycol; and a sweetener. See '271, claims 1, 3, 6, 8, 10, and 11. PEG 400 is used in the examples that are defined in the specification. See instant claim 27. As for the new limitation of claim 11, it is viewed that the pharmacokinetic property of the present composition is obviously present in the patented product which comprises the same type of solvents and another benzodiazepine active ingredient used for the same purposes.

While the patent claims a nasal formulation for lorazepam and a method of treating anxiety-related disorders by using the composition, the patent does not teach midazolam.

Schweizer teaches a method of treating panic disorder, panic attacks and the prevention of panic attacks to reduce anxiety by nasally administering midazolam and its pharmaceutically acceptable salts. See instant claim 3. The reference teaches administering 1-4 drops of an aqueous solution of midazolam, which is equivalent to 0.05-0.2 ml of the active ingredient. See col. 4, lines 41 – 53; instant claims 4 and 7. The reference teaches a nasal suspension in col. 3, lines 63- 66, meeting instant claim 7. Inducing general anesthesia by administering midazolam with other anesthetic agent is also taught. See col. 3, lines 8 – 10; instant claims 8 and 15. The reference teaches that a relatively low dosage of midazolam is required for the treatment, and that the drug is well tolerated and easily administered. See col. 5, line 46 – col. 7, line 24.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the '271 invention by substituting lorazepam with midazolam because 1) both are art-recognized equivalents since they are well known anxiolytic drugs which are intranasally administered; and 2) Schweizer teaches that midazolam nasal spray is effective even in low dosage, well tolerated and easily administered. The skilled artisan would have had a reasonable expectation of successfully producing a similar nasal composition for reducing anxiety. It is also viewed that the obvious variation of the prior arts, which would comprise midazolam in a nasal carrier comprising polyethylene glycol and propylene glycol as required by the present invention, would naturally have the metabolism rate as defined in the present claims 16-19.

Claims 17, 20, and 28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 8-11, 19, 21, 23, 24, and 27 of '271 and Schweizer as applied to claims 11-15, 18, and 27 as above, and further in view of Fisgin et al. (J. of Child Neurol. Dec. 2000).

The '271 patent and Schweizer does not teach the time required for midazolam to take effects.

Fisgin discloses a method of rapidly treating acute seizures of children in 5 minutes by nasally administering midazolam (5 mg/mL). See abstract.

It would have been obvious to a skilled artisan to formulate and administer the midazolam nasal spray of the combined references as motivated by Fisgin because the latter teaches the time required for midazolam that is nasally administered to take

effects. The skilled artisan would have had a reasonable expectation of successfully determining the dosage of midazolam and the time required to treat acute by nasally administering midazolam.

Claim 29 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 8-11, 19, 21, 23, 24, and 27 of '271 and Schweizer as applied to claims 11-15, 18, and 27 as above, and further in view of Knoester et al. (Br. J. Clin. Pharmacol. 53, 501-507).

The combined references fail to teach a midazolam intranasal composition comprising no less than 25 mg/ml of midazolam or its salts.

Knoester teaches administering intranasal preparation comprising 5mg/mL in a mixture of water and propylene glycol. See p. 502, Methods. The reference teaches that the dose of intranasal midazolam for treating seizure activity is based on body weight, and increasing the concentration of midazolam reduces the total volume of fluid to be delivered, thereby maintaining the bioavailability and efficacy of the drug. See p. 502, first column, first 2 paragraphs.

It would have been obvious to one of ordinary skill in the art to modify the teachings of the combined references by increasing the concentration of midazolam or its salts as motivated by Knoester, because the latter teaches that increasing the midazolam concentration to meet the required dose is more effective than increasing the amount of the fluid.

Claims 11-15, 18, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Pat. Application No. 11/376979 in view of Schweizer (US 5,166,202).

The '979 application claims a sedative-anxiolytic nasal composition comprising lorazepam; 15-25 % by volume of polyethylene glycol 400 and 75-85 % by volume of propylene glycol. As for the new limitation of claim 11, it is viewed that the pharmacokinetic property of the present composition is obviously present in the product of the copending application, which comprises the same type of solvents and another benzodiazepine active ingredient used for the same purposes.

The copending application does not claim a midazolam nasal composition.

Schweizer is discussed above.

It would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the '979 invention by substituting lorazepam with midazolam because 1) both are art-recognized equivalents since they are well known anxiolytic drugs which are intranasally administered; and 2) Schweizer teaches that midazolam nasal spray is effective even in low dosage, well tolerated and easily administered. The skilled artisan would have had a reasonable expectation of successfully producing a similar nasal composition for reducing anxiety. It is also viewed that the obvious variation of the prior arts, which would comprise midazolam in a nasal carrier comprising polyethylene glycol and propylene glycol as required by the present invention, would naturally have the metabolism rate as defined in the present claims 16-19.

Claims 17, 20, and 28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of '979 application and Schweizer as applied to claims 11-15, 18, and 27 as above, and further in view of Fisgin et al. (J. of Child Neurol. Dec. 2000).

The copending application and Schweizer do not teach the time required for midazolam to take effects.

Fisgin discloses a method of rapidly treating acute seizures of children in 5 minutes by nasally administering midazolam (5 mg/mL). See abstract.

It would have been obvious to a skilled artisan to formulate and administer the midazolam nasal spray of the combined references as motivated by Fisgin because the latter teaches the time required for midazolam that is nasally administered to take effects. The skilled artisan would have had a reasonable expectation of successfully determining the dosage of midazolam and the time required to treat acute by nasally administering midazolam.

Claim 29 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of '979 application and Schweizer as applied to claims 11-15, 18, and 27 as above, and further in view of Knoester et al. (Br. J. Clin. Pharmacol. 53, 501-507).

The combined references fail to teach a midazolam intranasal composition comprising no less than 25 mg/ml of midazolam or its salts.

Knoester teaches administering intranasal preparation comprising 5mg/mL in a mixture of water and propylene glycol. See p. 502, Methods. The reference teaches that the dose of intranasal midazolam for treating seizure activity is based on body weight, and increasing the concentration of midazolam reduces the total volume of fluid to be delivered, thereby maintaining the bioavailability and efficacy of the drug. See p. 502, first column, first 2 paragraphs.

It would have been obvious to one of ordinary skill in the art to modify the teachings of the combined references by increasing the concentration of midazolam or its salts as motivated by Knoester, because the latter teaches that increasing the midazolam concentration to meet the required dose is more effective than increasing the amount of the fluid.

Oath/Declaration

Applicant's declaration filed on November 7, 2008 has been fully considered. The declarant/applicant states that the time to achieve maximum plasma concentration (Tmax) of midazolam administered intranasally in a formulation comprising polyethylene glycol and propylene glycol as recited in the present claims would not have been predictable in view of the cited prior arts at the time of the present invention. Since applicant has amended the claims to recite the Tmax of midazolam and the solvents including the weight amount of polyethylene glycol, examiner views applicant's argument commensurate with the scope of the claim and persuasive.

Response to Arguments

Applicant's arguments filed on November 7, 2008 have been fully considered and are persuasive in part. The claim rejections made under 35 U.S.C. 103 (a) have been withdrawn in view of the claim amendment.

Response to Arguments

Applicant's arguments filed on January 31, 2008 have been fully considered but they are not persuasive in part and moot in view of new grounds of rejection in part.

Applicant argues that each of the references fails to disclose using about 15-25 % by volume of polyethylene glycol. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that '832 teaches away from using about 15 -25 % by volume of polyethylene glycol. The argument is unpersuasive because it is viewed that there is no significant or nonobvious difference between up to about 10 % and the lower limitation of the claimed range, about 15 %.

Applicant argues that '375 patent and Fisgin fail to disclose midazolam and a formulation containing 15-25 % by volume of polyethylene glycol. The argument is unpersuasive because these limitations have been addressed by the primary reference and the '832 patent.

Applicant also argues that one of ordinary skill in the art would not have added midazolam to the carrier of the '832, '375, and '639 patents because these teach using ingredients other than midazolam. The argument is unpersuasive because the issue is whether adding the presently claimed glycol solvent and carrier to the invention of Schweizer, the primary reference, would have been obvious. The contents of the formulations of the secondary references need not be incorporated into the midazolam nasal spray of Schweizer. Furthermore, applicant's claims do not exclude the presence of ingredients other than midazolam.

Applicant's argument regarding claim 29 is moot in view of the new rejections made above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINA C. YU whose telephone number is (571)272-8605. The examiner can normally be reached on Monday through Friday, from 9:00AM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gina C. Yu/
Primary Patent Examiner, Art Unit 1611